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DIAGNOSIS OF SICKLING BY PLACENTAL EXAMINATION

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Diagnosis of sickling by placental examination

Geographic differences in incidence

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When the placenta separates from the uterine wall, the resulting hypoxia creates a natural sickling preparation of the trapped erythrocytes in the placenta. A histologic examination of 2,117 consecutive placentas from Negro women enrolled in the Collaborative Study showed a sickling incidence of 9.4 per cent. Sickling rates in the southern institutions (11.0 to 12.2 per cent) were higher than in the northern institutions (6.1 to 8.4 per cent). It is postulated that these geographic differences in sickling rates may indicate increased admixture of Caucasian blood among northern Negroes. Permanent histologic sections of the placenta offer the advantages of retrospective study, uniformity of technique, and reconfirmation of diagnosis which are not possible with sickle-cell preparations on peripheral blood.

WHEN THE placenta separates from the uterine wall the resulting hypoxia creates a natural sickling preparation of the trapped erythrocytes within the placenta. With the usual histopathologic methods of tissue processing and fixation the sickling state is maintained in the delivered placenta, providing an excellent tool for the diagnosis of sicklemia. Using peripheral blood smears, the incidence of sicklemia in Negroes as reported in different parts of the United States varies from 5.0 to 14.0 per cent.[1, 2, 4, 5] The cause for such wide variation is not clear but could be due to differences in technique of preparation as well as in the number of cases sampled. On the other hand, it could also be a true geographic difference. The Collaborative Study seems especially suitable for the evaluation of such differences since the placentas of all study women from institutions in various parts of the country were examined histologically.

From the Perinatal Research Branch, National Institute of Neurological Diseases and Blindness, National Institutes of Health.

The Collaborative Study of Cerebral Palsy, Mental Retardation and Other Neurological and Sensory Disorders of Infancy and Childhood is supported by the National Institute of Neurological Diseases and Blindness. The following institutions participate: Boston Lying-in Hospital; Brown University; Charity Hospital of New Orleans; Children's Hospital of Buffalo; Children's Hospital of Philadelphia; Children's Medical Center, Boston, Columbia University; The Johns Hopkins University; Medical College of Virginia; New York Medical College; Pennsylvania Hospital; University of Minnesota; University of Oregon; University of Tennessee; Yale University; and the Perinatal Research Branch, National Institute of Neurological Diseases and Blindness.

Material and methods

About 300 consecutive placentas from Negroes were sampled from each of seven different institutions enrolled in the Collaborative Study. A total of 2,117 placentas was examined microscopically for sickled erythrocytes without foreknowledge of the clinical diagnosis. The sections examined were 3 cm. wide and spanned the entire thickness of the placenta. The institutions selected were: Charity Hospital (New Orleans, Louisiana), University of Tennessee (Memphis, Tennessee), Medical College of Virginia (Richmond, Virginia),

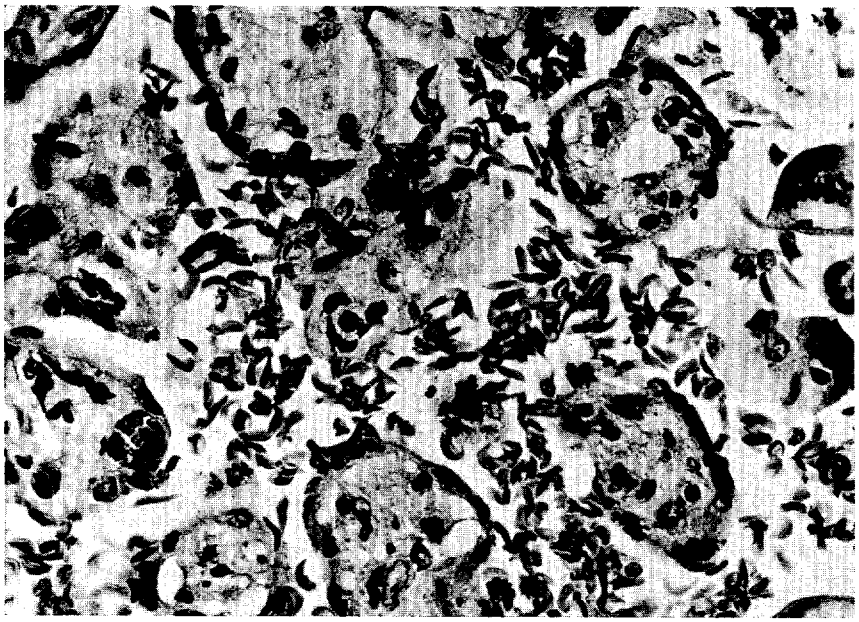

Fig. 1. Sickled maternal erythrocytes in placental intervillous spaces. (×400.)

The Johns Hopkins Hospital (Baltimore, Maryland), Pennsylvania Hospital (Philadelphia, Pennsylvania), New York Medical College (New York, New York), and University of Oregon (Portland, Oregon). The five other institutions were excluded from this study because of the paucity of Negro registrants or because the fixative used for the placenta was not suitable for this study. Ten per cent formalin was the best fixative for this purpose and was used by the seven institutions. Zenker's solution was unsatisfactory because of the presence in the solution of an oxidizing agent which appeared to cause reversal of the sickling phenomenon, and Bouin's fixative caused undue hemolysis. For the diagnosis of maternal sickling, only those showing moderate or marked sickling of erythrocytes in the intervillous spaces were considered as positive cases (Fig. 1). Borderline cases showing a few sickled erythrocytes were classified under the normal group.

Results and comments

As a diagnostic and genetic tool for sickling, the placenta, which is a natural sickling preparation, seems to produce fewer artifacts than the artificial sickling preparations. With the abundance of maternal erythrocytes in the intervillous spaces the diagnosis can be made fairly easily and rapidly. Because they are permanent sections, retrospective studies can also be done which are not possible with sickle cell preparations of peripheral blood.

The over-all incidence of sicklemia among pregnant Negroes in the Collaborative Study population based on this study was 9.4 per cent (Table I). It is interesting to note that the sickling rates in the southern institutions (11.0 to 12.2 per cent) were higher than in the northern institutions (6.1 to 8.4 per cent). This difference was statistically significant ($P < 0.002$ by chi square test). The sickling rates based on placental examination compared favorably with the data on peripheral blood examination of the United States Negroes as reported in the literature. The reported incidences range from 14.2 per cent (of 500 pregnant Negroes in South Carolina[5]) to 7.9 per cent (of 2,011 pregnant Negroes in Memphis[1]). Margolies[4] reported 7.2 per cent as the over-all incidence of sickling in the United States Negroes. The lower incidence of sick-

Table I. Sickling in maternal blood of negroes by histologic examination of the placenta

Location of institution	*No. of consecutive placentas examined*	*No. with sickling*	*%*
Southern			
New Orleans	309	34	11.0
Memphis	336	41	12.0
Richmond	316	35	11.1
Central			
Baltimore	348	32	9.2
Northern			
Philadelphia	309	26	8.4
New York	311	19	6.1
Portland	188	12	6.4
Total	2,117	199	9.4

ling among northern Negroes in our study suggests increased admixture of Caucasian blood in this group. This apparent geographic difference tends to be supported by the results of a preliminary analysis of ABO blood groups and Rh types in the Collaborative Study population (Table II). The difference in the frequency distributions of blood groups A and B in the northern Negro (26.4 per cent A, 19.9 per cent B) is closer to that of the white (38.9 per cent A, 10.9 per cent B) than is that of the southern Negro (24.8 per cent A, 21.8 per cent B). Likewise, the frequency of Rh-negative Negro women appears to be higher in the northern institutions (7.3 per cent) than in the southern institutions (5.8 per cent). However, Glass and Li[3] reported a frequency distribution of the ABO blood groups of Negroes in Baltimore, which did not substantially differ from that of Negroes in North Carolina as reported by Snyder or from that presented by Landsteiner and Levine of Negroes in New York. The significance of our findings on blood groups and types in our own population will require further investigation including genotype analysis.

Table II. Percentage distribution of ABO blood groups and frequency of Rh-negative cases in the Collaborative Study population

	Whites	*Northern Negroes**	*Southern Negroes†*
Total No. of cases examined	7,980	4,100	2,893
Rh negative	15.4	7.3	5.8
A	38.9	26.4	24.8
B	10.9	19.9	21.8
AB	3.7	4.0	3.2
O	46.5	49.7	50.2

*Boston, Providence, New York, and Philadelphia.
†New Orleans, Memphis, and Richmond.

Sickling determination is an interesting epidemiological method to test the dynamics of racial intermixture in United States Negroes. Retrospective analysis of sickling based on examination of placentas of Negroes from different parts of the United States has raised the possibility that geographic differences in sickling rates may represent true genetic differences.

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